REMARKS

Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are currently under consideration.

1. The Claims Are Not Obvious in View of Minden, Nelson or Barry

The rejection of claims 1-11,13-14,17-18, 21, and 24-27 is maintained under 35 U.S.C. §103(a) as being unpatentable over Minden et al. WO 02/086081 A2 ("Minden") and Nelson et al. U.S. Patent 6,887,713 ("Nelson").

According to the Examiner, Minden teaches methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden is said to further teach (i) that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized; (ii) that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location; (iii) that the total protein content of a cell or tissue can be utilized as the protein mixture; (iv) that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin; (v) that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues; (vi) that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids; (vii) that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents; (viii) that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture; (ix) that the array can have 2-100 different proteins; (x) that the binding reagents can be antibodies; (xi) that the proteins are compared to a reference set (i.e. characterizing; (xii) that the reference set can include prediction about binding based on the predicted digests of a protein mixture; (xiii) that various binding reagents can be compared to a reference set or to other binding reagents.

According to the Examiner, although Minden does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry, for present claims 1, 24, and 26, Nelson teaches analyzing complex biological mixtures utilizing "lab-on-a-chip" (i.e. chip-based microarrays) and MALDI-

TOF (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry) wherein the proteins are quantified (i.e. abundance), internal reference standards are utilized, and determining the amount (i.e. abundance) of the proteins. According to the Examiner, the claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF) would have yielded predictable results to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

The rejection of claims 1-11, 13-14, 17-18, 21, 24, and 26-27 is maintained by the Examiner under 35 U.S.C.§ 103(a) as being unpatentable over Minden and Barry et al. WO 0225287 ("Barry"). Barry is said by the Examiner, to teach methods of determining the binding and mass of trypsin digested proteins including antibodies from a cell including phage or tissue sample immobilized on an array. According to the Examiner, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of identifying proteins taught by Minden with the MALDI-TOF analysis taught by Barry.

Applicant maintains that, for reasons detailed below, the present invention is not render obvious by Minden, Nelson or Barry, either alone or in combination. Applicant has amended the claims to specify that (i) the heterogenous sample of proteins, peptides, protein fragments or peptide fragments bind to antibodies or fragments thereofi, each antibody or fragment thereof, fixed to spaced apart defined locations on an array; and (ii) wherein those proteins, peptides, protein fragments or peptide fragments binding to a specific antibody represent a heterogenous class and the members of each class have a motif common to that class. Further, as set forth in the claims as amended the bound proteins, peptides, protein fragments or peptide fragments are characterized using mass spectrometry.

As previously set forth by Applicant, in Minden's method the sample of proteins is deposited in spots. The antibodies are then added one-by-one and if the binding motif is present, the antibody will bind specifically to the spot. Thus, information will only be obtained regarding whether the antibodies bound the spots or not as it is the bound antibody that is detected. As

soon as ≥2 proteins/spot are deposited, i.e. in all cases when a mixture of proteins is targeted, one cannot determine to which of all the deposited proteins in each spot the antibody bound to, as binding motifs can be shared between different proteins. Hence, no information about the composition of the sample is generated.

In contrast to the method of Minden, in the presently claimed method it is the antibodies that are deposited one by one in unique spots. A sample of peptides/proteins is added to the array of immobilized antibodies. Mass spectrometry is subsequently used to determine which peptides/proteins are bound to each antibody, i.e. it is the bound peptides/proteins that are detected. Hence, crude mixtures can be addressed and information about the sample composition can be generated.

With regard to Nelson and Barry, Applicant maintains that neither reference supplies the disclosure that is absent from Minden. Nelson discloses "a method and device for the capture and subsequent digestion or derivatization of an analyte" (See, col. 4, lines 41-43). As depicted in Figure 1 of Nelson, the analyte appears to be a single homogeneous molecule. Further, as indicated previously, Barry only teaches a method of proteomic analysis wherein each binding reagent corresponds to one protein and requires advanced knowledge of proteins in the sample in order to generate an appropriate array of binders. In other words, Barry, like Nelson, only teaches the determination of abundance wherein the analysis is applied to homogeneous classes of array-bound proteins. Both the teachings of Barry and Nelson are in contrast to the present invention which relates to a method of determining the mass and abundance of a heterogeneous class of array-bound peptides, or protein or peptide fragments. Applicant maintains that, indeed, it is the basis of the present invention to provide a means for complex sample evaluation with relatively small arrays.

Applicant maintains that combining the teachings of Minden and Nelson or Minden and Barry will not provide the same end-results as provided by the presently claimed invention, because the disclosed methods are fundamentally different. Minden discloses a method that is used to select and/or eliminate specific binders (whether the method of Barry or Nelson is used) while the present invention is utilized to analyse the composition of complex protein-based heterogeneous constituents. It is noteworthy that the method of Minden (whether combined with the method of either Barry or Nelson) will simply not give the same end results as the present invention.

Thus, the combined teachings of Minden and Nelson, and Minden and Barry, are conceptually different and not interchangeable with the claimed invention and would give strikingly different end results. Hence, the claims are non-obvious over the combination of Minden and Nelson and, therefore, the rejection under 35 U.S.C. §103 should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is believed that the subject claims are in condition for allowance, which action is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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